[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Novel Derivatives of Docosahexaenoylethanolamide as Therapeutics for Neuronal Disorders

Description of Technology: This technology provides derivatives of Docosahexaenoylethanolamide (synaptamide or DEA) which have increased potency and hydrolysis resistance as compared to DEA (structures of these derivatives are available upon request), as well as methods of using these derivatives to promote neurogenesis, neurite growth, and/or synaptogenesis. Docosahexaenoic acid (DHA), an n-3 polyunsaturated fatty acid that accumulates in the brain during development, has been shown to play a key role in learning and memory development. Studies have also shown that DEA, a metabolite derived from DHA is very potent in accelerating neuronal growth and development. The inventors have discovered that the novel DEA derivatives they have designed are even more potent than DEA or DHA in accelerating neuronal growth, synaptogenesis and development. The inventors have shown that treatment of progenitor neural cells with some of these novel DEA derivatives leads to an increase in the amount of somatic neurons produced after differentiation. These novel compounds can be developed as therapeutics for conditions such as trauma, stroke, multiple sclerosis, Alzheimer's disease, brain and spinal cord injuries, and peripheral nerve injuries for rehabilitation.

Potential Commercial Applications:

• Agents to promote neurogenesis, neurite growth, and synaptogenesis.

• Therapeutics for neurological conditions, such as traumatic brain injury, spinal cord injury, peripheral nerve injury, stroke, multiple sclerosis, autism, Alzheimer’s disease, Huntington’s disease, Parkinson’s disease, and amyotrophic lateral sclerosis.

Competitive Advantages: These derivatives of DEA provide increased potency and hydrolysis resistance compared to DEA.

Development Stage:

• Prototype

• Early-stage

• Pre-clinical

• In vitro data available

Inventors: Erika Englund (NCATS), Juan Marugan (NCATS), Samarjit Patnaik (NCATS), Hee-Yong Kim (NIAAA)

Publications:

1. Kim HY, et al. N-Docosahexaenoylethanolamide promotes development of hippocampal neurons. Biochem J. 2011 Apr 15;435(2):327-36. [PMID 21281269]

2. Kim HY, et al. A synaptogenic amide N-docosahexaenoylethanolamide promotes hippocampal development. Prostaglandins Other Lipid Mediat. 2011 Nov;96(1-4):114-20. [PMID 21810478]

3. Cao D, et al. Docosahexaenoic acid promotes hippocampal neuronal development and synaptic function. J Neurochem. 2009 Oct;111(2):510-21. [PMID 19682204]

Intellectual Property: HHS Reference No. E-070-2012/0 — U.S. Provisional Application No. 61/624,741 filed 16 Apr 2012

Licensing Contact: Suryanarayana (Sury) Vepa, Ph.D., J.D.; 301-435-5020; vepas@mail.nih.gov

Collaborative Research Opportunity: The National Center for Advancing Translational Sciences is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please contact Dr. Juan Marugan at maruganj@mail.nih.gov or Dr. Krishna Balakrishnan at balakrik@mail.nih.gov.

High-Affinity Rabbit Monoclonal Antibodies To Mesothelin for Treatment of Cancer

Description of Technology: Mesothelin is a cell surface protein that is highly expressed in aggressive cancers, such as malignant mesothelioma, ovarian cancer and pancreatic cancer. Because of this selective expression, mesothelin is an excellent candidate for targeted therapeutics, such as monoclonal antibodies (mAbs) and chimeric molecules. Current anti-mesothelin therapeutic mAb candidates bind to an epitope in Region I of mesothelin. Unfortunately, Region I contains the interaction site MUC16/CA125, a mesothelin-interacting protein that is present in the serum of patients with mesothelin-related cancers. Because the current therapeutic mAb candidates must compete with MUC16/CA125 for binding to mesothelin, they may not reach their full therapeutic potential due to interference.

In order to address this concern, NIH inventors generated several rabbit mAbs that recognize unique epitopes of mesothelin: (1) YP223, which recognizes region II; (2) YYP218, which recognizes region III; and (3) YP3 which recognizes a native conformation epitope of mesothelin. These mAbs bind to mesothelin with sub-nanomolar affinity and are not out-competed for binding by the current anti-mesothelin therapeutic

mAb candidates or MUC16/CA125. This strong binding affinity for an alternative binding site on mesothelin suggests that these mAbs are excellent therapeutic candidates.

Potential Commercial Applications:

• Therapeutic use, such as treatment of mesothelin-expressing cancers as a stand-alone mAbs or as a mAb-drug conjugate (e.g., an immunotoxin)

• Diagnosis of mesothelin-expressing cancers

• Antibody-related research use, including immunoprecipitation, western blot analysis, immunohistochemistry, ELISA, etc.

Competitive Advantages:

• Binding of new epitope on mesothelin may improve therapeutic applications due to non-competition from serum proteins

• High binding affinity (sub-nanomolar levels) also increases chances of binding and subsequent therapeutic activity

Development Stage:

• Early-stage

• In vitro data available

Inventors: Mitchell Ho et al. (NCI)

Publication: Ho M. Advances in liver cancer antibody therapies: a focus on glypican-3 and mesothelin. BioDrugs. 2011 Oct 1;25(5):275-84. doi: 10.2165/11595360-000000000-00000. [PMID 21942912]

Intellectual Property: HHS Reference No. E-198-2012/0 — U.S. Provisional Patent Application No. 61/691,719 filed 21 Aug 2012

Related Technologies:

• HHS Reference No. E-021-1998/0 — U.S. Patent 6,809,184 issued 26 Oct 2004

• HHS Reference No. E-139-1999/0 — U.S. Patent 7,081,518 issued 25 Jul 2006

• HHS Reference No. E-091-2009/0 — U.S. Patent Publication US 20120107933

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@mail.nih.gov

Collaborative Research Opportunity: The NCI Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize new monoclonal antibodies to unique domains of mesothelin for cancer therapy or diagnostics. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Single Domain Human Monoclonal Antibodies To Mesothelin for Treatment of Cancer

Description of Technology: Mesothelin is a cell surface protein that is highly expressed in aggressive cancers such as malignant mesothelioma, ovarian cancer and pancreatic cancer. This selective expression makes mesothelin an excellent candidate for targeted therapeutics such as monoclonal antibodies (mAbs) and corresponding chimeric molecules. Unfortunately, current anti-mesothelin mAb candidates have drawbacks, such as competition with a serum protein (MUC16/CA125) for binding to mesothelin, the formation of neutralizing antibodies because they are non-human antibodies, and the inability to trigger complement-dependent cytotoxicity (CDC).

In order to address this concern, NIH inventors generated two single domain human mAbs: SD1 and SD2. SD1 recognizes a unique epitope in region III of

mesothelin which is not out-competed for binding by MUC16/CA125. SD1 was also capable of triggering CDC, as well as antibody-dependent cellular cytotoxicity (ADCC). Due to its human origin, SD1 is also less likely to elicit the formation of neutralizing antibodies when administered to patients. Each of these characteristics suggests SD1 may be an effective therapeutic agent. Indeed, SD1 was able to inhibit tumor growth in mouse xenograft models, and corresponding immunotoxins were able to inhibit tumor cell growth in vitro, supporting the use of SD1 as a therapeutic mAb.

Potential Commercial Applications:

• Therapeutic use, such as treatment of mesothelin-expressing cancers as a stand-alone mAbs or as a mAb-drug conjugate (e.g., an immunotoxin)

• Diagnosis of mesothelin-expressing cancers

• Antibody-related research use, including immunoprecipitation, western blot analysis, immunohistochemistry, ELISA, etc.

Competitive Advantages:

• Binding of a new epitope on mesothelin may improve therapeutic applications due to non-competition from serum proteins

• Human origin may significantly limit the formation of neutralizing antibodies, thereby increasing therapeutic potential of the mAb

• Ability to trigger both CDC and ADCC may elicit a more complete therapeutic response

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Mitchell Ho et al. (NCI)

Publication: Ho M. Advances in liver cancer antibody therapies: a focus on glypican-3 and mesothelin. BioDrugs. 2011 Oct 1;25(5):275-84. doi: 10.2165/11595360-000000000-00000. [PMID 21942912]

Intellectual Property: HHS Reference No. E-236-2012/0 — U.S. Provisional Patent Application No. 61/706,396 filed 27 Sep 2012

Related Technologies:

• HHS Reference No. E-021-1998/0 — U.S. Patent 6,809,184 issued 26 Oct 2004

• HHS Reference No. E-139-1999/0 — U.S. Patent 7,081,518 issued 25 Jul 2006

• HHS Reference No. E-091-2009/0 — U.S. Patent Publication US 20120107933

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@mail.nih.gov

Collaborative Research Opportunity: The NCI Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize single-domain human antibodies (SD1 and SD2) to mesothelin for cancer therapy or diagnostics. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

January 23, 2013
Date

_____

Richard U. Rodriguez,
Director
Division of Technology Development and Transfer
Office of Technology Transfer
National Institutes of Health

[FR Doc. 2013-01789 Filed 01/28/2013 at 8:45 am; Publication Date: 01/29/2013]